American Journal of Medical Genetics (Neuropsychiatric Genetics) 74:218–219 (1997)

Letter to the Editor

Wiskott-Aldrich Syndrome in Two Sisters

To the Editor:

We previously published the paper entitled, "Two Sisters With Clinical Diagnosis of Wiskott-Aldrich Syndrome: Is the Condition in the Family Autosomal-Recessive?" [Kondoh et al., 1995]. Briefly, we described 2 sisters in a family representing manifestations of Wiskott-Aldrich syndrome (WAS). The older sister had suffered from recurrent infections, small-sized thrombocytopenia, petechiase and purpura, and eczema for 7 years. The younger sister had the same manifestations, and died of intracranial bleeding at age 2 years. All the laboratory data on the 2 patients and the result of the sialophorin analysis were compatible with WAS, although they were females. Polymerase chain reaction (PCR) analysis of the sialophorin gene and single-strand conformation polymorphism (SSCP) analysis of the PCR product demonstrated that there were no detectable size-changes or electrophoretic mobility changes in the DNA from both parents. Studies on the mother-daughter transmission of the X chromosome using a pERT84-*Mae*III polymorphic marker mapped at Xp21, and HPRT gene polymorphism at Xq26, suggested that each sister had inherited a different X chromosome from the mother.

We subsequently tried reverse-transcriptase (RT)-PCR analysis against the WASP gene of our patient's peripheral lymphocyte to elucidate whether the older sister had any mutations in the WASP gene. We used two sets of PCR primers which overlay the coding region of the WASP cDNA [Derry et al., 1994]. The sequences and locations of the primers are WASP1F: 5′-CAGAGAAGACAAGGGCAGAA-3′, nucleotide position 9–28; WASP1R: 5′-TAAGTTTAGAGGTCTCGGCG-3′, nucleotide position 883–902; WASP2F: 5′-AGATCTGCGGAGTCTGTTCT-3′, nucleotide position 829–848; and WASP2R: 5′-ACAGGGCAGCAAGTAACTCA-3′, nucleotide position 1546–1565. As shown in Figure 1, there is no detectable size-change.

Next, we performed parental-origin analysis of chromosome 16 of DNAs in this family to make clear whether the aberration of the sialophorin gene, including the noncoding region, caused our patients' disorder. We used seven set of primers, i.e., D16S402, D16S403, D16S404, D16S406, D16S407, D16S420, and the sialophorin CA repeat, located on chromosome 16.

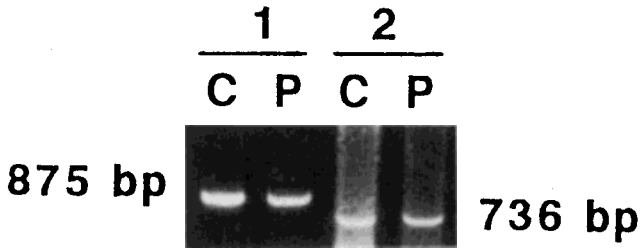

Fig. 1. RT-PCR analysis in a normal control (C) and the older sister (P). **Lanes 1** and **2** indicate WASP1F-WASP1R and WASP2F-WASP2R, respectively.

Among these sets, only one set of primers, the sialophorin CA repeat, was informative (Fig. 2). The father and the older sister were heterozygous for alleles A and B. On the other hand, the mother and the younger sister were homozygous for allele A. This suggested that each sister had inherited a different chromosome 16 from at least their father.

In our previous paper, we suggested three explanations for the occurrence of WAS in our patients. First, they had an autosomal gene mutation whose function was similar to that of the WASP gene. Second, they may have had a mutation in an autosomal gene that may have regulated the WASP gene, and therefore the mutation of the former resulted in the reduction of the latter. Third, there remains the possibility that they may have had a point mutation in the sialophorin gene, especially at the promoter region, which could not be de-

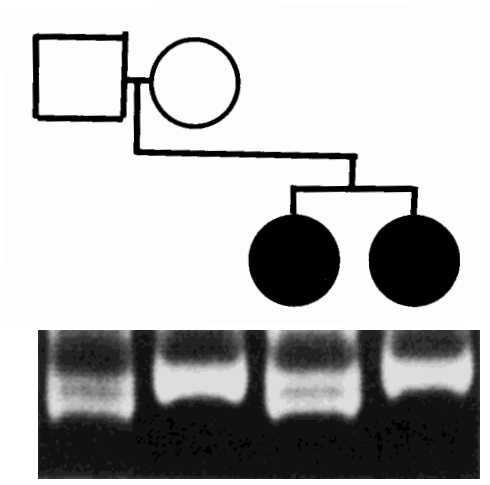

Fig. 2. Parental-origin examination of chromosome 16 using the sialophorin CA repeat polymorphism. The father, mother, patient 1, and patient 2 were heterozygous for AB, homozygous for A, hetrozygous for AB, and homozygous for A, respectively.

*Correspondence to: Tatsuro Kondoh, M.D., Ph.D., Department of Pediatrics, Nagasaki University School of Medicine, 1-7-1, Sakamoto-machi, Nagasaki City, Nagasaki 852, Japan.

Received 9 July 1996; Revised 11 July 1996

tected by SSCP analysis. Based on our present study, we can dismiss the third possibility. Recently, Symons et al. [1996] reported that the Wiskott-Aldrich syndrome protein functions as an effector for the GTPase CDC42Hs to actin polymerization and cytoskeletal rearrangement. Our case may have a deficiency in this pathway exclude the WASP.

REFERENCES

Derry JMJ, Ochs HD, Francke U (1994): Isolation of a novel gene mutated in Wiskott-Aldrich syndrome. Cell 78:635–644.

Kondoh T, Hayashi K, Matsumoto, T, Yoshimoto M, Morio T, Yata J, Tsuji Y (1995): Two sisters with clinical diagnosis of Wiskott-Aldrich syndrome: Is the condition in the family autosomal recessive? Am J Med Genet 60:364–369.

Symons M, Derry JMJ, Karlak B, Jiang S, Lemahieu V, McCormick F, Francke U, Abo A (1996): Wiskott-Aldrich syndrome protein, a novel effector for the GTPase CDC42Hs, is implicated in actin polymerization. Cell 84:723–734.

Tatsuro Kondoh*
Tadashi Matsumoto
Yoshiro Tsuji
Department of Pediatrics
Nagasaki University School of Medicine
Nagasaki, Japan